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Foley & Lardner
3000 K Street N W Suite 500
Washington, DC 20007-5109

EXAMINER

KWON, BRIAN YONG S

ART UNIT	PAPER NUMBER
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1614

12

DATE MAILED: 10/28/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/807,603

Applicant(s)

TODO, SATORU

Examiner

Brian S Kwon

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 August 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-53 and 57-105 is/are pending in the application.
- 4a) Of the above claim(s) 1-34, 50-53, 58-100, 102, 103 and 105 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 35-47, 49 and 57 is/are rejected.
- 7) ☒ Claim(s) 46, 48, 101 and 104 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 April 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5. 6) ☐ Other: _____

DETAILED ACTION**Election Acknowledged**

1. Applicants election with traverse, in Paper No. 11, the Group B-I, claims 41, 48, 59 and 104, together with claims 35-40, 42-47, 49, 57 and 101, is acknowledged. Applicants traverse the restriction requirement on the grounds that the special technical linking the claimed invention is sPLA2 inhibition activity exhibited by compounds of formula I-XXIII, not the compounds of formula I-XXIII. This argument is not persuasive, as the prior art clearly discloses the claimed compounds represented by the formula as sPLA2 inhibitors. For example, EP 675110 discloses the claimed inodole-3-glyoxylamides represented by the formula as sPLA2 inhibitors or a composition comprising the claimed inodole-3-glyoxylamides having sPLA2 inhibitors. Similarly, EP 620214, EP 675110, US 5986106, US 5733923, US 5919810, Draheim et al. (J. Med. Chem., 1996, 29(26), 5159-5175), WO 9603376. WO 9603383, WO 96/031120, WO 9603383, WO 9721664, WO 9721716, WO 9818464, WO 9824437. WO 9824756, WO 9824794, WO 9825609, US 5453443, EP 887342, WO 9847507, and WO 9837069 disclose (i) the claimed compounds represented by the formula as sPLA2 inhibitors and/or (ii) a composition comprising the claimed compounds, sPLA2 inhibitors, represented by the formula and/or (iii) methods of using the compositions comprising the claimed compounds, sPLA2 inhibitors, represented by the formula.

As stated in the reason of the record, the technical feature relating each group of claims to the other does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art. Thus, the requirement is deemed proper, and made Final.

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Acknowledgment is made of applicants election of [[3-(2-amino-1,2-dioxoethyl)-2-ethyl-1-(phenylmethyl)-1H-indole-4-yl]oxy]acetic acid sodium salt as the elected species, which reads on formula (I) structure compounds. In applicants Response, applicants state that claims 35-49, 57, 59, 101 and 104 read on this species. However, claim 59 (which is represented by Formula (IV) structure) does not read on the elected species (see definition of R_A substituents, wherein R_A is attached to nitrogen (indole)). Therefore, claim 59 will be withdrawn from further consideration by the examiner, 37 CFR 1.142(b), along with 1-34, 50-53, 58, 60-100, 102, 103 and 105, as being drawn to a non-elected claims.

Claims 35-49, 57, 101 and 104 are currently pending for the examination.

Drawings

2. The drawings filed August 8, 2000 are objected to by the Draftsperson under 37 CFR 1.84 or 1.152. Applicant is requested to notice the box 3 and 12 made by the Draftsperson. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Claim Objections

3. Claim 46 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 38. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

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Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 35-49, 57, 101 and 104 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 35-36, 38-43, 45-49, 57, 101 and 104 are incomplete and unclear by omitting active step such as the subject that the claimed sPLA2 inhibitor is administered to.

Claims 37 and 44 are incomplete and unclear by omitting active step such as the subject (e.g., organ) that the claimed preservation solution comprising a sPLA2 inhibitor is contacted to. It appears in view of the specification (page 25, lines 1-8) that the claimed method is achieved by contacting an organ whose directly connected arteries or veins being ligated at an operation or contacting an organ before organ transplantation extirpated from a donor to a recipient at a surgery for organ transplantation with a preservation solution comprising a sPLA2 inhibitor. However, applicant's omission of above-mentioned active step in claims 37 and 44 make the claims unclear.

5. Claim 45 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 45 recites a method for treating ischemia reperfusion injury, which comprises administering a sPLA2 inhibitor before the occurrence of ischemia caused by surgery or cardiac standstill. Although the claim language is definite, the interpretation of the claim renders the

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claim indefinite. In view of the whole context of the claim 45, the instant claim could be interpreted as (i) the prophylactic use of sPLA2 inhibitor in the treatment of ischemia reperfusion injury and (ii) the use of sPLA2 inhibitor in subject with existing ischemia reperfusion injury prior to (re)occurrence of ischemia.

Applicants recitation of “before the occurrence of ischemia caused by surgery or cardiac standstill” with “treating ischemia reperfusion injury” renders the claim uncertain of its category of the invention. In view of the differences of the scope of protection which may be attached to the various categories of claims, it must be ensured that wording of a claim leaves no doubt as to its category.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 35-40, 42-47 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Sonnino et al. (Digestive Diseases and Sciences, Vol. 42, No.5, May 1997).

The reference discloses PX-13 as a sPLA2 inhibitor, and it further states that PLA2 released during ischemia is a type-II substance, that sPLA2 contributes to ischemic reflow, and that control of sPLA2 activity protects tissue fragments from ischemia and reflow in cold preservation graft study. More specifically, it describes remedies or preventives for ischemic

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reflow damage containing PLA2 inhibitors (Abstract; page 977, column 1, lines 13-18 and page 980, column 1, lines 1-13).

The teaching of Sonnino clearly anticipates the claimed invention except “before the occurrence of ischemia” in claim 36 and “before reperfusion of blood to an organ” in claim 37. However, such features are non-limiting to the interpretation of the instant claims since the administration (or contacting) of sPLA2 inhibitor such PX-13 to the subject (e.g., organ) would have a protective utility as the claimed invention regardless of “before the occurrence of ischemia” or “before reperfusion of blood to an organ”. In other words, the referenced prophylactic utility of sPLA2 inhibitor (e.g., PX-13) in ischemia reperfusion injury must be present at all times when the sPLA2 inhibitor is administered to the subject. Therefore, regardless “before the occurrence of ischemia” or “before reperfusion of blood to an organ”, the referenced teaching of administering sPLA2 inhibitor possessing such protective utility clearly anticipates the claimed invention.

7. Claim 41 is rejected under 35 U.S.C. 102(b) as being anticipated by Khau et al. (US 5986106)

Khau teaches the use of [[3-(2-amino-1,2-dioxoethyl)-2-ethyl-1-(phenylmethyl)-1H-indole-4-yl]oxy]acetic acid and its sodium salt as sPLA2 inhibitor for treating septic shock (column 1, lines 10-14; column 12, line 52; Example 1) .

The claim read on a method for preventing ischemia reperfusion injury, comprising administering sPLA2 inhibitor represented by formula (I).

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Although the reference is silent about the use of the claimed sPLA2 inhibitor represented by the formula (I) for preventing ischemia reperfusion injury, administering of the referenced sPLA2 inhibitor such as [[3-(2-amino-1,2-dioxoethyl)-2-ethyl-1-(phenylmethyl)-1H-indole-4-yl]oxy]acetic acid to the subject inherently possesses the claimed protective utility of preventing ischemia reperfusion injury. Therefore, the reference clearly anticipates the claimed invention.

Claim Rejections - 35 USC §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
 2. Ascertaining the differences between the prior art and the claims at issue.
 3. Resolving the level of ordinary skill in the pertinent art.
 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
8. Claim 45 is rejected under 35 U.S.C. 103(a) as obvious over Sonnino et al. (Digestive Diseases and Sciences, Vol. 42, No.5, May 1997).

The teaching of Sonnino has been discussed in above 35 USC 102(b) rejection.

The claim differs from the reference by “before the occurrence of ischemia caused by surgery or cardiac standstill”.

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With respect to the prophylactic use of sPLA2 inhibitor in the treatment of ischemia reperfusion injury, Sonnino clearly teaches the prophylactic use of sPLA2 inhibitor in ischemia-reperfusion injury as discussed in above 35 USC 102(b) rejection.

With respect to the use of sPLA2 inhibitor in subject with existing ischemia reperfusion injury prior to (re)occurrence of ischemia, One having ordinary skill in the art would have been motivated to administer known sPLA2 inhibitor (e.g., XP-13), with the reasonable expectation of success, to treat existing ischemia reperfusion injury “before the occurrence of ischemia caused by surgery or cardiac standstill”. One having ordinary skill in the art would have expected that XP-12 having sPLA2 inhibiting activity would be useful in the treatment of ischemia reperfusion injury before the occurrence of ischemia.

Allowable Subject Matter

9. The following is a statement of reasons for the indication of allowable subject matter:

Bach et al. (US 5654326; WO 98/18464; WO 96/03120; WO 96/03376; EP 0620214; EP 0620215; EP 0675110) teaches the use of the claimed 1H-indole-3-glyoxylamide derivatives as a sPLA2 inhibitor for the treatment of septic shock, adult respiratory distress syndrome, pancreatitis, trauma, bronchial asthma, allergic rhinitis, rheumatoid arthritis and etc.

Khau et al. (US 5986106) teaches the use of [[3-(2-amino-1,2-dioxoethyl)-2-ethyl-1-(phenylmethyl)-1H-indole-4-yl]oxy]acetic acid and its sodium salt sPLA2 inhibitor for treating septic shock.

Gemba et al. (US 6214855) teaches the use of the claimed compounds (e.g., [[3-(2-amino-1,2-dioxoethyl)-2-ethyl-1-(phenylmethyl)-1H-indole-4-yl]oxy]acetic acid, [[3-(2-amino-

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1,2-dioxoethyl)-2-methyl-1-(phenylmethyl)-1H-indol-4-yl]oxy] acetic acid, 2-[[3-(2-amino-1,2-dioxoethyl)-2-methyl-1-(phenylmethyl)-1H-indol-4-yl]oxy] propanoic acid and [[3-(2-amino-1,2-dioxoethyl)-2-cyclopropyl-1-(phenylmethyl)-1H-indol-4-yl]oxy] acetic acid and its sodium salt) for the treatment of stroke.

However, none of prior art references teach or suggest the use of the claimed sPLA2 inhibitor represented by Formula (I) for treating (or preventing) ischemia reperfusion injury.

Claims 48, 101 and 104 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

10. No Claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703)308-5377. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

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Brian Kwon

ZOHREH FAY
PRIMARY EXAMINER
GROUP 1600

A handwritten signature in cursive script, appearing to read "Zohreh Fay", written in black ink.